IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

'09 CIV 2555

SHIRE CANADA INC., SHIRE INTERNATIONAL LICENSING B.V., and SHIRE US INC.,

Plaintiffs,

- v -

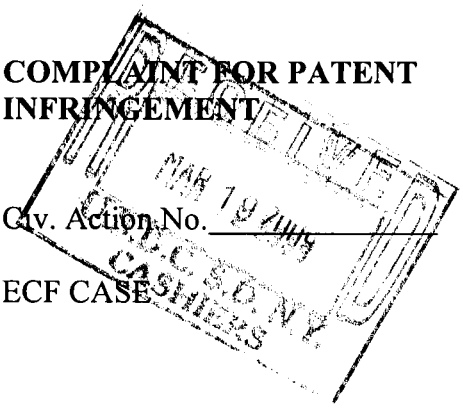
MYLAN INC., MYLAN PHARMACEUTICALS INC., and MATRIX LABORATORIES LIMITED,

Defendants.

COMPLAINT FOR PATENT INFRINGEMENT

Civ. Action No._____

ECF CASE



Plaintiffs Shire Canada Inc., Shire International Licensing B.V., and Shire US Inc. (collectively, "Shire"), by their attorneys, for their complaint against Mylan Inc., Mylan Pharmaceuticals Inc., and Matrix Laboratories Limited, allege as follows:

The Parties

1. Plaintiff Shire Canada Inc. is a corporation organized and existing under the laws of Canada and has a principal place of business at 2250, boul. Alfred-Nobel, bureau 500, Ville St-Laurent, QC H4S 2C9, Canada.

2. Plaintiff Shire International Licensing B.V. is a corporation organized and existing under the laws of the Netherlands and has a principal place of business at Strawinskylaan 847, 1077 XX Amsterdam, Noord-Holland, The Netherlands.

3. Plaintiff Shire US Inc., is a corporation organized and existing under the laws of New Jersey and has a principal place of business at 725 Chesterbrook Blvd., Wayne, PA 19087, United States.

4. Upon information and belief, Defendant Mylan Inc. is a corporation organized and existing under the laws of Pennsylvania and has a principal place of business at 1500 Corporate Drive, Canonsburg, PA 15317.

5. Upon information and belief, Defendant Mylan Pharmaceuticals Inc. is a corporation organized and existing under the laws of West Virginia and has a principal place of business at 781 Chestnut Ridge Road, Morgantown, WV 26505.

6. Upon information and belief, Defendant Matrix Laboratories Limited ("Matrix") is a corporation organized and existing under the laws of India and has a principal place of business at 1-1-151/1, 4th Floor, Sai Ram Towers, Alexander Road, Secunderabad – 500 003, Andhra, Pradesh, India.

Jurisdiction and Venue

7. This is a civil action for patent infringement arising under the patent laws of the United States, Title 35 of the United States Code, for infringement of United States Patent No. 5,968,976 ("the '976 patent"). This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

8. Mylan Inc. is subject to personal jurisdiction in this judicial district by virtue of, *inter alia*, having conducted business in the State, having availed itself of the rights and benefits of New York law, and having engaged in substantial and continuing contacts with the State. In addition, upon information and belief, Mylan Inc. operates an office in New York, at the following address: 405 Lexington Ave, New York, NY 10174. Moreover, Mylan Inc. has made counterclaims in the United States District Court for the Southern District of New York in connection with other lawsuits.

9. Mylan Pharmaceuticals Inc. is subject to personal jurisdiction in this judicial district by virtue of having conducted business in the State. In addition, upon information and belief, Mylan Pharmaceuticals Inc. has made counterclaims in the United States District Court for the Southern District of New York in connection with other lawsuits.

10. Matrix is subject to personal jurisdiction in this judicial district by virtue of the fact that Mylan Inc. and Mylan Pharmaceuticals Inc. are designated U.S. agents of Matrix, and that Mylan Inc. is a corporate parent of Matrix. In addition, upon information and belief, Matrix has conducted business in the State.

11. Venue is proper in this judicial district pursuant to 28 U.S.C. §§ 1391 and 1400(b).

Regulatory Requirements for Approval of New and Generic Drugs

12. Any person wishing to market a pioneering drug – that is, a new drug that has not previously been approved by the Food and Drug Administration ("FDA") – must first file a New Drug Application ("NDA") with FDA demonstrating that the drug is safe and effective for its intended use. 21 U.S.C. § 355(b). To secure approval of a NDA, the NDA applicant must, among other things, collect and submit to FDA extensive animal and human clinical trial data at a substantial cost of time and money.

13. A person wishing to market a generic copy of a pioneering drug that previously has been approved by FDA may follow a truncated approval process by filing an Abbreviated New Drug Application ("ANDA") for a generic version of the drug. In the ANDA, the applicant must demonstrate, among other things, bioequivalence

of the generic copy of the pioneering drug. 21 U.S.C. § 355(j)(2)(A)(iv). To demonstrate bioequivalence, the ANDA applicant must show that the rate and extent of absorption of the therapeutic ingredient in the generic drug does not significantly differ from that in the pioneering drug, or, if the rate of absorption differs, that such difference is intentional, is reflected in the proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug. 21 U.S.C. § 355(j)(8)(B).

14. However, unlike a NDA applicant, an ANDA applicant is not required to include safety and effectiveness data. The ANDA applicant is not required, for example, to conduct well-controlled clinical trials concerning the safety and effectiveness of the proposed drug. Instead, the ANDA applicant is permitted to piggy-back on the safety and effectiveness data developed and submitted by the approved NDA holder. 21 U.S.C. § 355(j).

15. Nor does an ANDA applicant establish any new conditions of use for the proposed drug product. Instead, an ANDA applicant may seek approval only for conditions of use that previously have been approved in connection with an approved NDA. 21 U.S.C. § 355(j)(2)(A)(i).

16. No person may market in the United States a new drug without an approved NDA or a generic version of a drug without an approved ANDA. 21 U.S.C. § 355(a).

Plaintiffs' Approved Drug Product

17. Shire is the holder of an approved new drug application, NDA No. 21-468, for lanthanum carbonate chewable tablets. That NDA was approved for tablets

of Eq. 500 mg base on October 26, 2004, and for tablets of Eq. 750 mg base and 1000 mg base on November 23, 2005.

18. Pursuant to FDA's approval, Shire currently markets lanthanum carbonate chewable tablets for reduction of serum phosphate in patients with end stage renal disease under the trademark FOSRENOL®.

19. FDA has listed the '976 patent in the Orange Book – formally known as Approved Drug Products With Therapeutic Equivalence Evaluations – in connection with NDA No. 21-468.

20. The '976 patent qualifies for listing in the Orange Book in connection with NDA No. 21-468 because it claims an approved use of the drug product that is the subject of that NDA. Mylan Inc., Mylan Pharmaceuticals Inc., and Matrix Laboratories Limited (collectively, "Mylan") have never challenged the listing of this patent in the Orange Book.

Mylan's ANDA

21. Mylan has represented that on or before February 4, 2009, it submitted to FDA Matrix's ANDA (ANDA No. 90-976) and paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 355(j)(2)(A)(vii)(IV), for lanthanum carbonate chewable tablets purportedly bioequivalent to Shire's FOSRENOL® lanthanum carbonate chewable tablets. The purpose of the ANDA and paragraph IV certifications is to obtain approval under section 505(j) of the FDCA to engage in the commercial manufacture and sale of its proposed lanthanum carbonate chewable tablets before the expiration of the patents listed in the Orange Book for Shire's NDA No. 21-468. Hence, Mylan's purpose in

submitting ANDA No. 90-976 is to market in the United States the lanthanum carbonate products described therein before expiration of the '976 patent.

22. On or about February 4, 2009, Mylan sent a letter advising Shire of Mylan's paragraph IV certification relating to the '976 patent ("Mylan's Notice Letter"). Mylan's Notice Letter included an offer of confidential access that would permit Shire's outside counsel to review Mylan's ANDA, subject to conditions limiting its distribution and use.

23. Upon information and belief, the sole condition of use for which Mylan seeks approval in its ANDA No. 90-976 for its proposed lanthanum carbonate chewable tablets is the reduction of serum phosphate in patients with end stage renal disease, the same condition of use as that approved in Shire's NDA No. 21-468.

24. Upon information and belief, the sole indication set forth in the proposed labeling submitted by Mylan in its ANDA No. 90-976 for its proposed lanthanum carbonate chewable tablets is the reduction of serum phosphate in patients with end stage renal disease, the same indication as that set forth in the approved labeling for Mylan's FOSRENOL® lanthanum carbonate chewable tablet products.

Count 1: Patent Infringement – '976 patent

25. Shire realleges paragraphs 1 through 24 above as if fully set forth herein.

26. On October 19, 1999, the United States Patent and Trademark Office duly and legally issued the '976 patent, entitled "Pharmaceutical Composition Containing Selected Lanthanum Carbonate Hydrates." The term of the '976 patent runs

through October 26, 2018. A true and correct copy of the '976 patent is attached hereto as Exhibit A.

27. Shire is the owner of the '976 patent.

28. Shire currently markets lanthanum carbonate chewable tablets in the United States under the trademark FOSRENOL®. The product FOSRENOL® and the conditions of use for which FOSRENOL® is approved fall within one or more of the claims of the '976 patent.

29. Mylan is liable for infringement of the '976 patent under 35 U.S.C. § 271(e)(2)(A) by virtue of its filing ANDA No. 90-976 with a paragraph IV certification seeking FDA approval of ANDA No. 90-976 prior to expiration of the '976 patent.

30. The product for which Mylan seeks approval in its ANDA No. 90-976 falls within one or more of the claims of the '976 patent. If approved, the manufacture, use, offer for sale, and sale in the United States, and importation into the United States of Mylan's proposed lanthanum carbonate product would infringe one or more of the claims of the '976 patent.

31. Upon information and belief, if ANDA No. 90-976 is approved, Mylan intends to manufacture, use, offer for sale, and sell in the United States, and import into the United States, the lanthanum carbonate product for which approval is sought in Mylan's ANDA No. 90-976.

32. The manufacture, use, offer for sale and sale in the United States, and importation into the United States of Mylan's proposed lanthanum carbonate product

would infringe one or more claims of the '976 patent, and Mylan would be liable for direct infringement under 35 U.S.C. § 271(a).

33. Mylan's manufacture, use, offer for sale or sale in the United States, or importation into the United States, prior to expiration of the '976 patent, of the lanthanum carbonate products for which approval is sought in ANDA No. 90-976, would actively induce and contribute to infringement of the '976 patent, and Mylan would be liable as an infringer under 35 U.S.C. §§ 271(b) and/or (c).

34. Upon information and belief, the conditions of use for which Mylan seeks approval in its ANDA No. 90-976 fall within one or more of the claims of the '976 patent. Upon information and belief, if approved, use of Mylan's proposed lanthanum carbonate product in accordance with the proposed labeling submitted in ANDA No. 90-976 would infringe one or more of the claims of the '976 patent.

35. Upon information and belief, if approved, Mylan's proposed lanthanum carbonate products for which approval is sought in Mylan ANDA No. 90-976 will be administered to human patients in a therapeutically effective amount for reduction of serum phosphate in patients with end stage renal disease, which administration would constitute direct infringement of one or more claims of the '976 patent. Upon information and belief, this infringement will occur at Mylan's behest, with its intent, knowledge, and encouragement, and Mylan will actively induce, encourage, aid, and abet this administration with knowledge that it is in contravention of Shire's rights under the '976 patent.

36. Shire will be irreparably harmed if Mylan is not enjoined from infringing or actively inducing or contributing to infringement of the '976 patent. Shire does not have an adequate remedy at law.

Prayer For Relief

WHEREFORE, Plaintiffs seek the following relief:

A. A judgment that Mylan has infringed the '976 patent under 35 U.S.C. § 271(e)(2)(A);

B. A judgment and order pursuant to 35 U.S.C. § 271(e)(4) providing that the effective date of any FDA approval of ANDA No. 90-976 for lanthanum carbonate chewable tablets be not earlier than the expiration date of the '976 patent;

C. A judgment declaring that Mylan's manufacture, use, offer for sale, or sale in the United States, or importation into the United States, of the lanthanum carbonate products for which approval is sought in ANDA No. 90-976 would constitute infringement of the '976 patent, or would induce or contribute to such infringement, pursuant to 35 U.S.C. § 271 (a), (b), and/or (c);

D. A permanent injunction enjoining Mylan and its officers, agents, servants, and employees, and those persons in active concert or participation with any of them, from making, using, selling, or offering to sell in the United States, or importing into the United States, the lanthanum carbonate chewable tablets for which approval is sought in ANDA No. 90-976, or

any lanthanum carbonate product that infringes or induces or contributes to the infringement of the '976 patent, until expiration of that patent;

E. A finding that Mylan's paragraph IV certification is frivolous, a finding that this is an exceptional case, and an award of attorneys' fees in this action pursuant to 35 U.S.C. § 285;

F. An award of costs and expenses in this action; and

G. Such further and other relief as this Court determines to be just and proper.

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DATED: March 19, 2009

EXHIBIT A

US005968976A

United States Patent [19]

Murrer et al.

[11] Patent Number: 5,968,976

[45] Date of Patent: Oct. 19, 1999

[54] **PHARMACEUTICAL COMPOSITION CONTAINING SELECTED LANTHANUM CARBONATE HYDRATES**

[75] Inventors: **Barry A Murrer**; **Nigel A Powell**, both of Berkshire, United Kingdom

[73] Assignee: **AnorMed Inc.**, Langley, Canada

[21] Appl. No.: **08/913,960**

[22] PCT Filed: **Mar. 19, 1996**

[86] PCT No.: **PCT/GB96/00575**

§ 371 Date: **Jan. 2, 1998**

§ 102(e) Date: **Jan. 2, 1998**

[87] PCT Pub. No.: **WO96/30029**

PCT Pub. Date: **Oct. 3, 1996**

[30] **Foreign Application Priority Data**

Mar. 25, 1995 [GB] United Kingdom 9506126

[51] **Int. Cl.**° **A01N 55/02**

[52] **U.S. Cl.** **514/492**; 514/512; 424/715; 534/16

[58] **Field of Search** 534/16; 514/492, 514/512; 424/715

[56] **References Cited**

PUBLICATIONS

Yanagihara et al., "Synthesis of Lanthanide Carbonates", Journal of the Less–Common Metals, 167(2) pp. 223–232, 1991.

Patent Abstract of vol. 11, No. 371, (C–462), Dec. 3, 1987 & JP, A, 62 145024 (Asahi Chem Ind Co Ltd), Jun 29, 1987.

Chemical Abstracts, vol. 107, No. 26, Dec. 28, 1987, abstract No. 249009, Mincely et al., "Molten potassium pyrosulfate: reactions of lanthanum metal and six of its compunds", XP002010788, see abstract, Aust. J. Chem. 40(7), pp. 1309–1314, 1987.

Chemical Abstracts, vol. 104, No. 26, Jun. 30, 1986, abstract No. 236218, Mzareulisvili et al., "Study of interaction of lanthanum nitrate with alkali metal and ammonium carbonates", XP002010789, Soobshch. Akad. Nauk Gruz. 121(1), pp. 81–84, (1986).

Chemical Abstracts, vol. 87, No. 20, Nov. 14, 1977, abstract No. 161013, Oda et al., "Studies on the crystal water of lanthanum carbonates", XP002010790, Oita Daigaku Kyoikygakubu Kenku Kiyo, Shizen Kagaku, 4(5), pp. 1–6, 1975.

Primary Examiner—Dwayne C. Jones

Attorney, Agent, or Firm—Morrison & Foerster, LLP

[57] **ABSTRACT**

Selected lanthanum carbonate hydrates may be administered into the gastrointestinal tract, to treat hyperphosphataemia in patients with renal failure.

10 Claims, 4 Drawing Sheets

Fig. 1

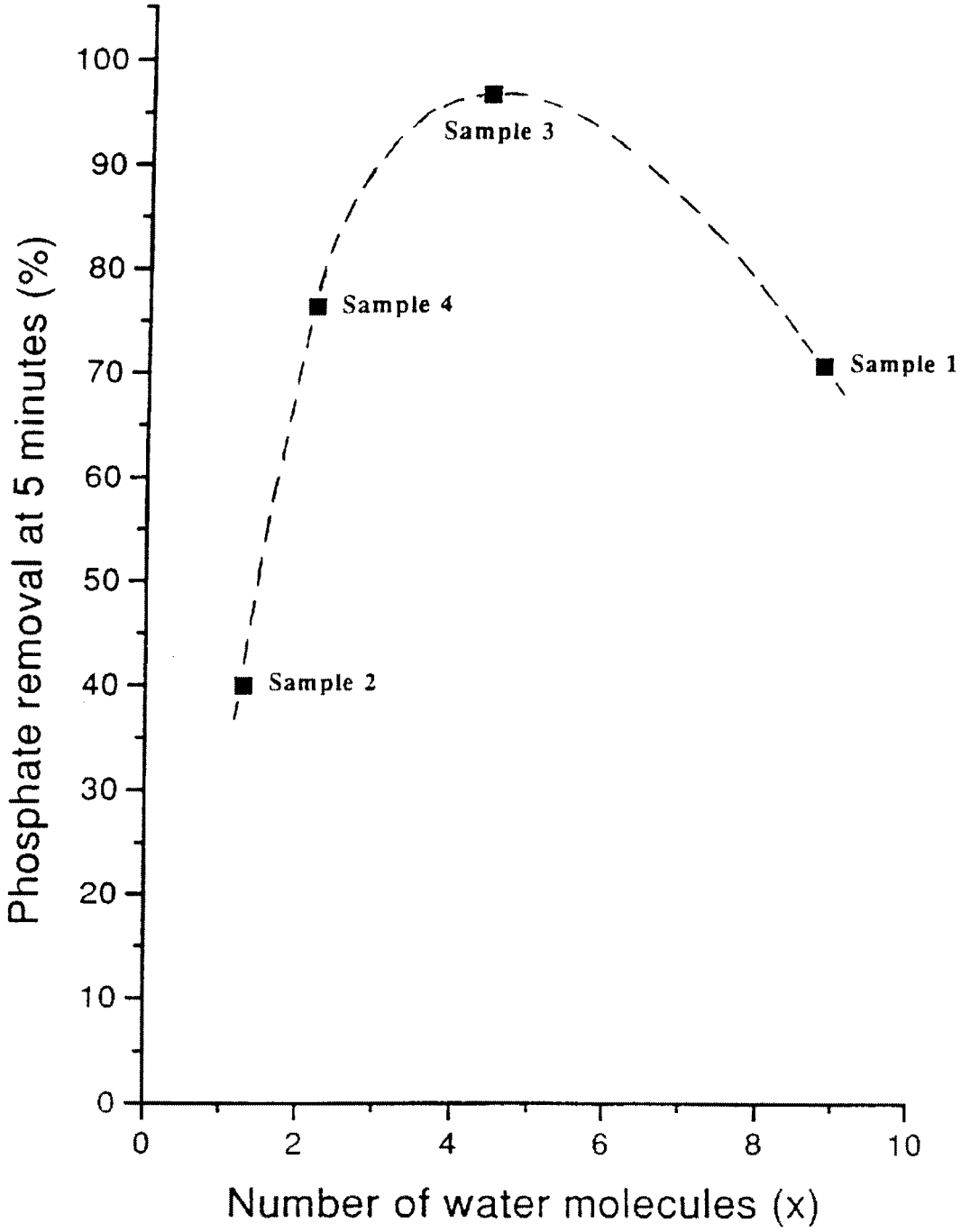

Phosphate removal at 5 minutes (%)
100
90
80
70
60
50
40
30
20
10
0
0
2
4
6
8
10
Number of water molecules (x)
Sample 3
Sample 4
Sample 1
Sample 2

Fig. 2

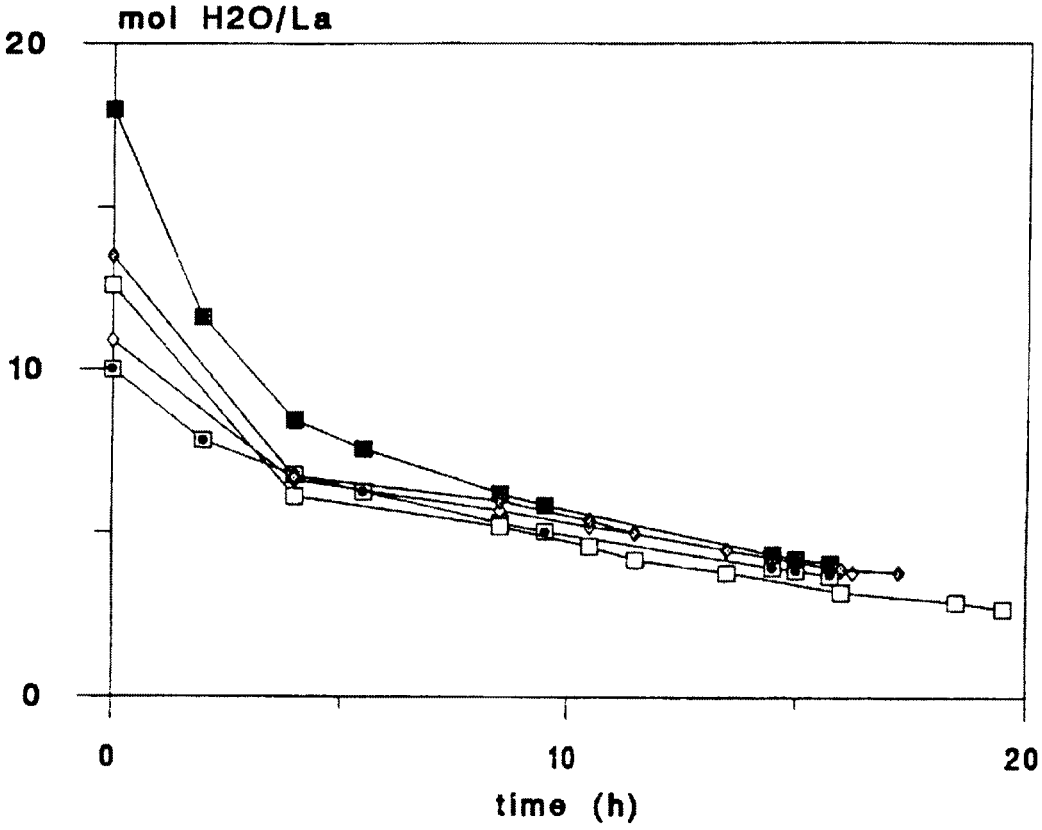


Fig. 3

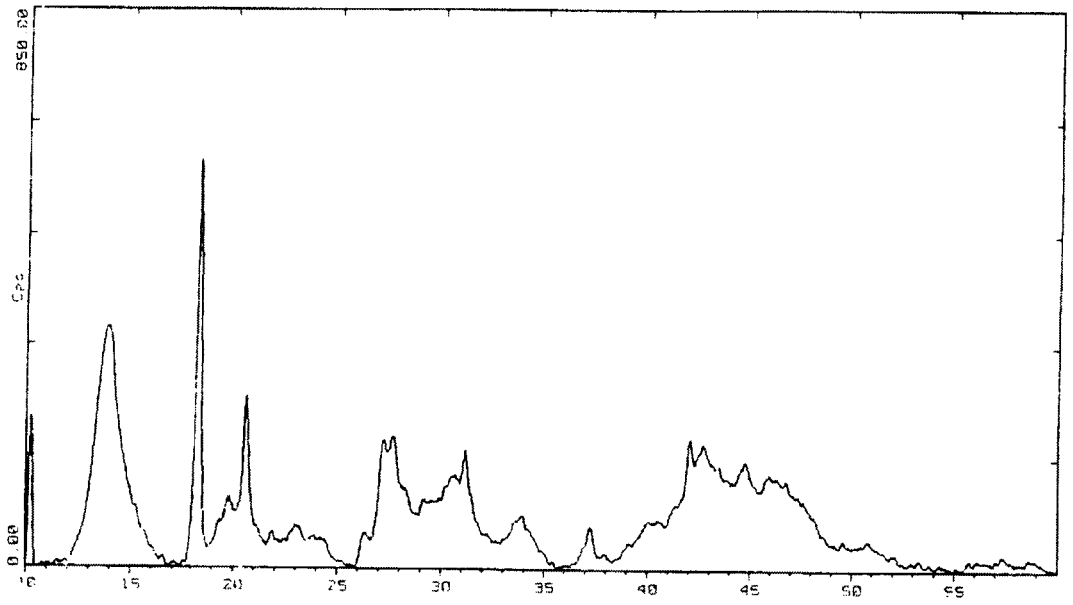
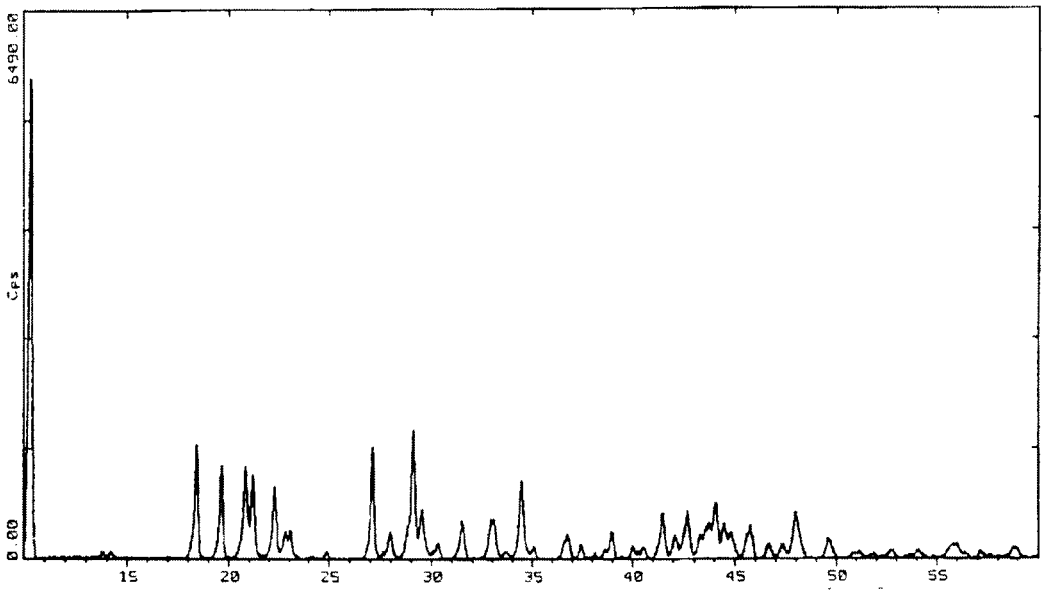


Fig.4



PHARMACEUTICAL COMPOSITION CONTAINING SELECTED LANTHANUM CARBONATE HYDRATES

This application is a 371 of PCT/GB96/00575 filed on Mar. 19, 1996.

This invention concerns a novel and inventive pharmaceutical composition and method, more particularly it concerns a composition for the treatment of hyperphosphataemia.

Hyperphosphataemia is a particular problem of patients with renal failure, using dialysis equipment. Conventional dialysis fails to reduce levels of phosphate in the blood, so that the levels rise in time. It is known to control phosphate levels by the oral administration of aluminium salts, or calcium salts. With the known toxic effects of aluminium, aluminium-based therapy tends to be avoided. In the case of calcium salts, calcium is absorbed rather readily from the gut, and in turn causes hypercalcaemia.

It has been suggested (Nakagawa et al, Trans Am Soc Intern Organs, 31, (1985) 155–9) that hydrous cerium oxide could be used as a bead in an ion-exchange column, to bind phosphate during dialysis. Japanese published patent application 61 004 529 appears to cover the same idea, suggesting that the hydrous oxides of La, Ce and Y may be used in the column. However, although the rare earths are generally considered of low toxicity according to the Hodge-Sterner classification system (Am Ind Hyg Assoc Quart, 10, (1943), 93), their toxicity when given iv, which corresponds to use in a blood dialysis system, is significant and we are not aware that the suggested ion exchange system or any development thereof has met with widespread acceptance or has been tested clinically for hyperphosphataemia.

It appears that cerium oxide or oxalate was administered many years ago for different medical indications, but that this has fallen into complete disuse.

Japanese published patent application number 62-145024 (Asahi Chemical Ind KK) discloses that rare earth carbonates, bicarbonates or organic acid compounds may be used as phosphate binding agents. One example of said published application relates to the use of lanthanum carbonate, although in the tests described, cerium organic acid salts and carbonate gave better phosphate ion extraction than lanthanum carbonate. Example 11 of said published application prepares $La_2(CO_3)_3.H_2O$, ie the monohydrate; all the other Examples are directed to rare earth carbonates other than lanthanum carbonate.

We have now discovered that certain forms of lanthanum carbonate exhibit improved performance in a variety of tests, over standard commercial lanthanum carbonate, which is believed to be the octahydrate form, and over $La_2(CO_3)_3.H_2O$ or similar compounds.

According to one aspect therefore, the present invention is the use of lanthanum carbonate of formula $La_2(CO_3)_3.xH_2O$ where x has a value from 3 to 6, preferably from 3.5 to 5, more especially from 3.8 to 4.5, for the preparation of a medicament for the treatment of hyperphosphataemia by administration into the gastrointestinal tract.

The invention further provides a pharmaceutical composition comprising said lanthanum carbonate, in admixture or association with a pharmaceutically acceptable diluent or carrier, in a form for administration into the gastrointestinal tract for the treatment of hyperphosphataemia.

The invention may also be expressed as a method of treatment of hyperphosphataemia in a patient with renal failure, comprising the administration of an effective dose of said lanthanum carbonate into the gastrointestinal tract.

According to another aspect, the present invention is a process for the preparation of lanthanum carbonate which comprises the steps of:

(i) reacting lanthanum oxide with an acid which gives a soluble salt of lanthanum;

(ii) reacting a solution of the thus obtained lanthanum salt with an alkali metal carbonate to produce a wet cake of lanthanum carbonate octahydrate; and

(iii) controlled drying of the wet cake of lanthanum carbonate octahydrate so as to obtain a lanthanum carbonate with 3 to 6 molecules of water of crystallisation.

According to yet another aspect, the present invention is lanthanum carbonate when obtained by the above-mentioned process.

According to a further aspect, the present invention is lanthanum carbonate of the formula $La_2(CO_3)_3.xH_2O$ where x has a value from 3 to 6.

BRIEF DESCRIPTION OF THE DRAWINGS

Embodiments of the present invention are described below, by way of example only, with reference to the accompanying drawings in which:

FIG. **1** illustrates the phosphate-binding capability of lanthanum carbonates having different degrees of water of crystallisation;

FIG. **2** illustrates the drying curves for five batches of lanthanum carbonate prepared by the method indicated in Example 1;

FIG. **3** illustrates the XRD analysis of lanthanum carbonate $4H_2O$ prepared by the method indicated in Example 2; and

FIG. **4** illustrates the XRD analysis of lanthanum carbonate $8.8H_2O$ of Sample 1 above.

For the tests described hereinafter, samples of lanthanum carbonate were obtained as follows:

Sample 1. Commercial lanthanum carbonate obtained from a chemical company.

This was characterised by elemental analysis (La, C, H), TGA, X-ray powder diffraction and ir spectroscopy, to have the formula $La_2(CO_3)_3.8.8H_2O$.

Samples 2–4 were prepared by heating portions of Sample 1 at varying temperatures for varying lengths of time, either under vacuum or at atmospheric pressure to obtain materials of formula $La_2(CO_3)_3.xH_2O$ where $0<x<8$.

Sample	Initial wt (g)	Temp (° C.)	Time (min)	Vacuum (Y/N)	Wt loss (g)	x
2	5.00	175	240	Y	1.09	1.3
3	20.0	80	180	N	2.6	4.4
4	5.01	100	720*	N	0.96	2.2

*Dried to constant weight.

Sample 5 is a sample of lanthanum carbonate which when analysed indicated a formula of $La(CO_3)_3.4H_2O$.

Sample 6 is a sample of lanthanum carbonate prepared according to Example 1 below and having the formula $La_2(CO_3)_3.3.8H_2O$.

In order to show that certain lanthanum carbonate hydrates are significantly different in phosphate binding activity from both lanthanum carbonate octahydrate and from $La_2(CO_3)_3.H_2O$, samples were tested as follows:

i) a stock solution was prepared by dissolving 13.75 g of anhydrous Na_2HPO_4, 8.5 g of NaCl in 1 litre deionised water.

ii) 100 ml of the stock solution was adjusted to pH3 by the addition of concentrated HCl.

iii) A 5 ml sample was taken and filtered through a 0.02 μm filter to give a Time 0 sample. This was analysed for phosphate using a Sigma Diagnostics Colorimetric Phosphorus test kit.

iv) 5 ml fresh stock solution was added to reestablish 100 ml, and the pH was re-adjusted to approximately 3.

v) $La_2(CO_3)3.xH_2O$ as a dry powder was added in an amount according to the molecular weight of the particular hydrate, to give a two-fold molar excess of lanthanum over phosphate and stirred at room temperature.

vi) Sampling was carried out at time intervals from 0.5 to 10 minutes, and the percentage of phosphate was determined as in iii) above. The results are shown in the Table 1 below.

TABLE 1

TIME	% PHOSPHATE REMOVED Sample					
(Minutes)	1	2	3	4	5	6
0						
0.5		13.4	18.8	15.1	22.9	31.4
1	29	18.4	31.5	26.8	40.4	55.5
1.5		25.4	43.1	36	55.2	74.8
2		28.1	50.6	45.3	69.5	88.1
2.5		30.8	60.5	51.8	79.9	95.3
3		34.4	69	57.6	90.3	99.6
4						100
5	70.5	39.9	96.5	76.3	100	100
10	100	ND	99.1	ND	100	100

It can readily be seen from Table 1 that Sample 3 ($La_2(CO_3)_3.4.4H_2O$); Sample 5 ($La_2(CO_3)_3.4H_2O$) and Sample 6 ($La_2(CO_3)_3.3.8H_2O$ appreciably quicker than the $8.8H_2O$, $.1.3H_2O$ or $2.2H_2O$ forms. We believe that the results for $La_2(CO_3)_3.1.3H_2O$ are in agreement with the results shown in the above mentioned Japanese published patent application number 62-145024 where for $La_2(CO_3)_3.H_2O$, only 90% removal is shown after 120 minutes.

It can also be readily seen from FIG. 1 of the accompanying drawings that the highest phosphate removal is obtained with lanthanum carbonates having 3 to 6 molecules of water.

The present invention offers the possibility of binding phosphate without any incursion of lanthanum into the blood stream, where toxic effects can cause problems. The specified lanthanum carbonate has negligible absorption from the gut, as shown by the in vivo tests described below.

Throughout this document, the term "treatment" is intended to include preventative treatment.

Processes for preparing lanthanum carbonates according to the present invention are described by way of illustration in the following Examples 1 and 2.

EXAMPLE 1

Lanthanum oxide (1.5 kg, 4.58 mol) was suspended in water (5.5 litres) in a 20 litre flask. Nitric acid (Analar grade, 69%, SG 1.42, 1.88 litres, 29.23 mol) was added to the stirred solution over 1.5 hours at such a rate as to keep the temperature between 60–80° C. The resulting lanthanum nitrate solution was left to cool to room temperature and filtered. A solution of sodium carbonate (1.65 kg, 15.57 mol) in water (7.75 litres) was added to the stirred lanthanum nitrate solution over 45 minutes. At the end of the addition the pH of the suspension w as 9.74. The suspension was left overnight, filtered (Buchner funnel, 540 paper) and dried on the filter in a current of air for 30 minutes. The solid was then re-suspended in water, stirred for 40 minutes and filtered. This procedure was repeated to give a total of six washes, when the nitrate concentration in the filtrate was <500 ppm. The final material (4.604 kg) was divided between three Pyrex dishes and a sample from each analysed for water content. (By decomposition of weighed sample of ($La_2(CO_3)_3.xH_2O$ at 1050° C., 2 hours to La_2O_3). The dishes were then placed in a fan oven at 80° C. and the weight loss of each dish monitored until the material of the required degree hydration was obtained. The progress of the drying is shown below

Time	mol H_2O/La		
(hours)	Dish 1	Dish 2	Dish 3
3.50	10.9	13.5	12.6
12	5.7	6.0	5.2
14	5.3	5.4	4.6
16	4.9	5.1	4.3
17	4.4	4.6	3.8
19.5	3.8	4.0	3.2

Drying curves for five batches produced by this route are shown in FIG. 2.

$La_2(CO_3)_3.3.8H_2O$ from dish 1 was selected as Sample 6 for the phosphate binding tests set forth in Table 1.

EXAMPLE 2

The process of Example 1 was repeated but using hydrochloric acid (12.28M, 2.48 litres) in place of nitric acid to dissolve lanthanum oxide (1.5 kg). The yield of crude product after six washes was 4.378 kg. The product was divided in three approximately equal portions in Pyrex dishes and dried in a fan oven at 80° C. After 2 hours a sample was taken from each tray and water analysed by decomposition to lanthanum oxide as described above. These figures were used to calculate the weight loss needed to give material of the required composition. The time course of the drying process is shown below.

Time	mol H_2O/La		
(hours)	Dish 1	Dish 2	Dish 3
2	21.3	22.1	20.4
5.5	12.3	13.2	12.2
9	7.9	8.0	7.6
11.5	6.9	7.0	6.6
17	4.9	5.1	4.6
18.5	4.6	4.8	4.2
19.5	4.4	4.6	4.1
20	4.3	4.6	4.0

Samples were taken from each dish, combined and analysed. The following results were obtained:

	Found	Calculation for $La_2(CO_3)_3.4H_2O$
% La (gravimetric)	52.38%	52.4%
carbonate (titration)	5.76 mol/g	5.66 mol/g
H_2O (NMR)	13.06%	13.59%

The XRD analysis for lanthanum carbonate $4H_2O$ prepared by the method of Example 2 is illustrated in FIG. 3.

FIG. 4 illustrates the XRD of lanthanum carbonate $8.8H_2O$ and it is evident that it has a different crystalline structure from lanthanum carbonate $4H_2O$ prepared by the method of Example 2. The XRD analysis of lanthanum carbonate $4H_2O$ prepared by the method of Example 1 was similar to the XRD analysis of lanthanum carbonate $4H_2O$ prepared by the method of Example 2.

Pharmaceutical compositions for oral administration according to the invention may be formulated and manufactured using methods well known in the art. Suitable diluents or carriers are also well known. The compositions may desirably be in a dosage form, to provide a single daily dose, or a number of sub-daily dosages. Conventional pharmacological methods may be used to ascertain suitable dose levels. The level of phosphate in the food that an individual ingests is important. Daily dosages are indicated to be in the range 0.1 to 50 g, preferably about 0.5 to 15 g. Suitable forms for oral administration include solid forms such as tablets, capsules and dragees and liquid forms such as suspensions or syrups. In addition to diluents and carriers, it is conventional in the formulation of oral preparations to include non-active ingredients such as thickeners, taste-improving components and colouring agents. The said carbonate may also be coated or treated to provide delayed-release forms. Preferably, the required daily dosage is given in tablet form, eg chewable tablet form, to be taken with meals. A suitable daily dosage of about 2 g for 70 kg man, should be compared with a daily dosage of 20 g for a commercial calcium-based phosphate binding composition.

To demonstrate that the lanthanum carbonate of the invention (or lanthanum phosphate formed after binding to phosphate in the gut) is fully excreted and does not pass out of the gut into the circulation system when given orally, three rats were dosed with 20 mg/kg of $La_2(CO_3)_3.4H_2O$ (Sample 5) and kept in metabolic cages where faeces and urine could be collected. The results are shown in Table 2 below.

Animal No.	Time (hours)	% La Recovered
1	24	103.2
1	48	0.1
1	72	<0.2
1	Total	103.3
2	24	75.3
2	48	23
2	72	1.2
2	Total	99.5
3	24	93.8
3	48	10
3	72	0.1
3	Total	103.8

It can be seen that after 72 hours, all of the lanthanum has been excreted. In the urine samples, the amount of lanthanum was below detection limits. After the test, the rats were sacrificed, and kidney, liver and femur were analysed for lanthanum. In all cases, the amount of lanthanum was below 0.1 ppm.

We claim:

1. A pharmaceutical composition for the treatment of hyperphosphataemia comprising lanthanum carbonate of the formula

$$La_2(CO_3)_3.xH_2O$$

where x has a value from 3 to 6, in admixture with a pharmaceutically acceptable diluent or carrier in a form for administration to the gastrointestinal tract.

2. A composition according to claim **1**, wherein x has a value from 3.5 to 5.

3. A composition according to claim **2**, wherein x has a value from 3.8 to 4.5.

4. A composition according to any one of claims **1** to **3** in unit dosage form to provide from 0.1 to 20 g/day.

5. A process for the preparation of lanthanum carbonate as defined in any one of claims **1** to **3** which comprises the steps of:

(i) reacting lanthanum oxide with hydrochloric acid to obtain lanthanum chloride;

(ii) reacting a solution of the thus obtained lanthanum chloride with an alkali metal carbonate to produce a wet cake of lanthanum carbonate octahydrate; and

(iii) drying the wet cake of lanthanum carbonate octahydrate so as to obtain a lanthanum carbonate with 3 to 6 molecules of water of crystallisation.

6. A process as claimed in claim **5** wherein the alkali metal carbonate is sodium carbonate.

7. A method to treat hyperphosphataemia in a subject which method comprises administering to said subject an amount of lanthanum carbonate of the formula

$$La_2(CO_3)_3.xH_2O$$

wherein x has a value from 3 to 6 effective to treat said hyperphosphataemia.

8. The method of claim **7** wherein x has a value from 3.5 to 5.

9. The method of claim **8** wherein x has a value from 3.8 to 4.5.

10. The method of any of claims **7**–**9** wherein said administering is by an oral route.

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